The Boston Globe

Breast cancer drug hailed

Treatment found to curb relapses from rapid tumor

By Liz Kowalczyk, Globe Staff | October 20, 2005

Cancer researchers today published a report on one of the most dramatic advances in breast cancer treatment in decades, finding that the drug Herceptin reduced by half the risk that women with a fast-growing type of tumor would experience a relapse.

Two separate studies, done mostly in the United States and Europe, focused on the 15 percent to 25 percent of patients with a gene mutation known as HER2-positive, which makes their breast cancers particularly aggressive and resistant to treatment. One in three of these women relapse, and most of those will die. But when Herceptin was given to women with early-stage HER2-positive cancer after surgery, and combined with standard chemotherapy agents, their cancer was far less likely to return.

The success of Herceptin shows the promise of a new approach to cancer treatment -- identifying specific genetic mutations in different types of cancer and developing therapies targeted to patients with those mutations. The belief is that such targeted drugs will be more effective than broad therapies have been.

"The results are simply stunning," a leading oncologist, Dr. Gabriel Hortobagyi of MD Anderson Cancer Center in Houston, wrote in an editorial accompanying the studies in The New England Journal of Medicine.

Another breast cancer specialist, Dr. Harold Burstein of Dana-Farber Cancer Institute, said that "for our generation of researchers, this is the most dramatic reduction in risk we've seen with treatment for breast cancer" and that the results "establish a new standard of treatment." The drug's maker, Genentech, occasionally has paid Burstein to speak at meetings.

The findings were so significant that the clinical trials were stopped early, and women in the control group were offered Herceptin. After the researchers disclosed their preliminary data at a cancer meeting in May, doctors began prescribing Herceptin to women with early-stage HER2-positive breast cancer, meaning that it has not spread from their breast and lymph nodes.

Doctors have given Herceptin to women with advanced breast cancer, which has recurred and spread, since the 1990s. But this is the first time researchers have conducted large studies of women with early-stage HER2-positive cancer.

Genentech, the California biotechnology company that makes Herceptin, said that sales of the drug from July to September had soared 70 percent to $215 million, compared with the same period last year. The study results published today are expected to reach an even wider group of doctors and patients.

Genentech, along with the National Cancer Institute, funded one of the studies, primarily conducted in the United States. But the company did not participate in the study's design, or data collection and analysis, researchers said. Roche, Herceptin's European marketer, sponsored the other study.

It is rare for a cancer drug to show such dramatic results, doctors said; treatment often is considered successful if it extends a patient's life by even several months. But Herceptin has shown the most promising results since studies of tamoxifen a decade ago found a similar reduction in the risk of relapse for women with estrogen-positive breast tumors.

About 215,000 women in the US are diagnosed with breast cancer annually, and they are routinely tested for genetic mutations that might dictate treatment.

Herceptin, which women take for a year, is an antibody that attaches itself to the HER2 gene on tumors, inhibiting the tumor's ability to grow.

In one of the studies, conducted primarily in the United States with 3,676 patients with HER2-positive cancer, 33 percent of women treated with surgery and standard chemotherapy had their cancer come back within four years. But just 15 percent of women treated with Herceptin in addition to surgery and chemotherapy suffered a relapse.

In the European study, which followed patients for two years, 23 percent of women not receiving Herceptin relapsed, compared with 15 percent of women treated with Herceptin.

In other words, women taking Herceptin cut their relative risk of relapse in about half.

There are concerns: About 4 percent of the women who took Herceptin in the US trial suffered cardiac side effects, most often congestive heart failure, a gradual weakening of the heart over several years that can eventually be fatal.

Dr. Edith Perez of the Mayo Clinic Jacksonville and one of the researchers, said most of the women improved after their Herceptin treatment was complete.

Other doctors warned, however, that possible cardiac side effects could become more widespread as Herceptin is given to more women.

"We don't know at this point whether these are going to be permanent episodes of heart damage or transient," said Hortobagyi, of MD Anderson. "These studies were done on women carefully selected to have normal heart function. So the numbers of patients with heart failure will likely be much higher. We have an important education task ahead of us, to make sure physicians carefully select patients and collaborate closely with cardiologists."

The growing use of Herceptin also could push up healthcare costs. The cost of a year's worth of treatment is about $50,000 per patient, far more than the cost of standard chemotherapy. Doctors said that most US insurers cover the drug for women with early stage HER2-positive cancer.

Many doctors and breast cancer patients now are changing their treatment plans.

Viola Bernard, 56, of Salem, N.H., was diagnosed last year with HER2- positive breast cancer that had spread into some of her lymph nodes. Bernard had a mastectomy, then saw Burstein at Dana-Farber in February for the next phase of treatment: chemotherapy and radiation. "He explained that mine was very fast-growing cancer and not the kind they like to see," she said. "I'll never forget he said, 'There's a new drug that's being studied. I wish I could give it to you because it sounds very promising.' "

In May, Bernard was taking the chemotherapy drug Taxol, which caused her bone and joint pain, when researchers first reported Herceptin results at the annual meeting of the American Society of Clinical Oncology in Orlando.

Soon after Burstein returned, he stopped Bernard's Taxol, and when she finished radiation in August, started her on Herceptin. Like many women, she has not experienced side effects.

"I was really excited to get on this drug. It gave me the hope I really needed," said Bernard, who owns the Common Grounds Cafe in Methuen.

For others, the transition has not been as smooth.

Dr. Eric Winer, director of the Breast Oncology Center at Dana-Farber, said women who participated in the US trial had been mailed letters in the spring with the results. And for those in the trial's control group who had not been administered Herceptin, those results could be upsetting.

This was particularly the case for those women whose breast cancer had come back as the trials were being conducted.

"We certainly came across many, many patients who had questions and found decisions about what to do with the results very difficult," he said.

The biggest issue, he said, is for women who have not gotten Herceptin but whose chemotherapy treatment ended one or more years ago. The women in the studies got Herceptin close to when they received chemotherapy, which may be crucial.

Researchers said the next step is to look for other genetic markers in breast cancer patients that predict which women will respond to Herceptin and to find other drugs that block HER2 mutations to see whether they improve results even more. ■